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(71) Applicant (for all designated States except US): CLIN-
IGENETICS [FR/FR]; 1105, avenue Pierre Mendes
France, F-3000 Nîmes (FR).

(72) Inventors; and

(75) Inventors/Applicants (for US only): MARGUERIE,
Gérard [FR/FR]; 68, rue du Génie, F-94400
Vitry-sur-Seine (FR). BENHABLES, Nora [FR/FR]; 61,
boulevard de Sébastopol, F-75001 Paris (FR).

(74) Agents: BRESSE, Pierre et al.; 3, avenue de l'Opéra,
F-75001 Paris (FR).

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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: METHODS FOR IDENTIFYING THERAPEUTIC AGENTS OF ATHEROSCLEROTIC PLAQUE LESIONS

(57) Abstract: The present invention relates to a method for identifying therapeutic agents for reducing and monitoring the growth, erosion, rupture or stability of an atherosclerotic plaque comprising the analysis of the differential expression of at least two genes coding proteins chosen among Stearoyl CoA desaturase, Phosphatidic acid phosphate, and Phosphoinositide-specific-phospholipase-B1, eventually in association with the analysis of the differential expression of at least one gene coding a protein chosen in the group comprising Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl transferase, Sphingosin phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca++ binding protein and CD163.

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INTERNATIONAL SEARCH REPORT

national Application No

PCT/IB 03/06419

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68 A61K45/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, MEDLINE, BIOSIS, EMBASE, SEQUENCE SEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| Y | WO 01/62954 A (UNIV BRITISH COLUMBIA ;XENON GENETICS INC (CA); WISCONSIN ALUMNI R) 30 August 2001 (2001-08-30) page 5, line 15-21 page 5, line 26-29 page 6, line 28 -page 7, line 3 page 19, line 17-19 page 23, line 20-24 page 24, line 18,19 page 31, line 15-18 page 49, line 20-25 page 63, line 26-32 --- -/-- | 1-20 |

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *O* document referring to an oral disclosure, use, exhibition or other means
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- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

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Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Helliot, B

INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| Y | WO 02/063005 A (TOWNLEY DAVID J ;EMERLING BROOKE M (US); HAFALIA APRIL J A (US); I) 15 August 2002 (2002-08-15) claims 20,22,23,25,48 page 25, line 20-23 page 36, line 26,27 page 37, line 6-9 page 51, line 23,24 table 2 claim 22 | 1-20 |
| Y | US 5 756 291 A (GRIFFIN LINDA ET AL) 26 May 1998 (1998-05-26) table 1 | 19,20 |
| A | US 6 114 114 A (SEILHAMER JEFFREY J ET AL) 5 September 2000 (2000-09-05) tables 1-4 | 1-20 |
| P,X | US 2003/166903 A1 (INCYTE GENOMICS, INC) 4 September 2003 (2003-09-04) the whole document table 1 | 1-20 |
| P,X | US 2003/157082 A1 (MILLENNIUM PHARMACEUTICALS, INC) 21 August 2003 (2003-08-21) the whole document | 1-20 |
| P,X | US 2003/153018 A1 (MILLENNIUM PHARMACEUTICALS, INC) 14 August 2003 (2003-08-14) the whole document | 1-20 |

INTERNATIONAL SEARCH REPORT

International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 21
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 21

Present claim 21 relates to the use of a compound modulating the expression of at least two gene coding a protein chosen among stearyl CoA desaturase, phosphatidic acid phosphate and phosphoinositide-specific phospholipase B1.

However, in the absence of any indication as to the nature of the used compound (i.e. the application does not contain any example of compounds according to claim 21), a lack of clarity within the meaning of Art. 6 PCT arises to such an extent that a meaningful search of the claim is impossible.

Consequently, no search has been carried out for the said claim 21.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
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| US 2003153018 | A1 | 14-08-2003 | WO 03045229 A2 | 05-06-2003 |